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Recent Advance in Diagnostic Oral Medicine – A Review

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Abstract:- Oral medicine plays a pivotal role in diagnostic decision-making and the field has witnessed significant advancements over time, revolutionizing the way oral diseases are diagnosed and managed. Recent advancements in diagnostic oral medicine offer promising solutions for early detection and accurate diagnosis. These innovations include the use of salivary biomarkers, advanced imaging technologies, and artificial intelligence (AI). Early detection is crucial for improving patient outcomes. Saliva-based biomarkers, such as miRNAs and proteins, provide a non-invasive method for early detection. Imaging techniques like auto fluorescence imaging, Raman spectroscopy, and optical coherence tomography enhances the visualization of abnormal tissues. AI-powered tools, particularly deep learning algorithms, can analyze images and data to improve diagnostic accuracy. By combining these technologies, we can achieve earlier detection, more accurate diagnosis, and personalized treatment plans for oral cancer patients.

Keywords:- *Oral cancer, Biomarkers, Artificial Intelligence, Nanotechnology, Chemiluminescence, Brush Biopsy.*

I. INTRODUCTION

Early advancement from molecular biology, optical physics have moved from Laboratories to our Clinic and it combined together to enhance the way of diagnosis. The morbidity and mortality associated with oral disease are reducing with Advancement.1 Advances in diagnostic oral medicine are aimed at reducing Oral cancer, primarily oral squamous cell carcinoma (OSCC), continues to be a major cause of cancer related deaths worldwide, with the prognosis for many patients remaining poor due to late stage detection.

Despite advancements in treatment, early detection remains a challenge, as many cases are diagnosed at more advanced stages when the chances of successful treatment are reduced.2 Recent developments in diagnostic oral medicine are offering promising solutions to these challenges by focusing on improving the early detection and accuracy of oral cancer diagnosis. These innovations include the identification of minimally invasive biomarkers, the refinement of advanced imaging technologies, and the integration of artificial intelligence (AI) into diagnostic processes.3

II. AI POWERED PRECISION IN ORAL CANCER DIAGNOSIS

The integration of artificial intelligence (AI) into healthcare, particularly in the diagnosis and management of oral cancer (OC), is ushering in a transformative era for the field. AI, especially through advanced machine learning techniques like deep convolutional neural networks (CNNs), is demonstrating significant promise in revolutionizing how we detect, classify, and predict the outcomes of oral cancer.6 AI's ability to process and analyse vast amounts of complex data, including histopathological images, is providing insights that were previously beyond the reach of traditional diagnostic methods. One of the key advantages of AI is its capacity to identify subtle patterns and anomalies within histopathological images that may be overlooked by human pathologists. This heightened accuracy in early detection plays a critical role in identifying oral cancer in its nascent stages, allowing for timely interventions that could significantly improve patient prognosis. Early diagnosis is essential in oral cancer, as it is a disease where outcomes are often closely tied to how early it is detected. AI's ability to detect even minute discrepancies in tissue samples helps in making more accurate predictions, potentially saving lives by facilitating early treatment. 5

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➢ *Nanotechnology: A Revolutionary Approach to Cancer Diagnosis and Treatment*

Nanotechnology, the manipulation of matter on an atomic and molecular scale, is revolutionizing the field of cancer diagnosis and treatment. By harnessing the unique properties of nanomaterials, scientists are developing innovative approaches to detect cancer at its earliest stages, deliver targeted therapies, and improve patient outcomes. Nanoparticles, such as gold nanoparticles, quantum dots, and liposomes, can be engineered to target specific cancer cells, delivering drugs directly to the tumor site while minimizing damage to healthy tissues. These nanoparticles can also be used as contrast agents for imaging techniques like magnetic resonance imaging (MRI) and computed tomography (CT), enhancing the visualization of tumors. Additionally, nanotechnology is being explored for the development of biosensors, which can detect cancer biomarkers with high sensitivity and specificity. These sensors can be used to monitor disease progression and assess the effectiveness of treatment. Furthermore, nanomaterials are being investigated for their potential to modulate the immune response against cancer, stimulating the body's natural defenses to fight the disease. While significant progress has been made, challenges remain in terms of toxicity, bio distribution, and regulatory approval. However, with continued research and development, nanotechnology holds the promise of transforming cancer care, leading to earlier diagnosis, more effective treatments, and improved patient survival rates.6,7

➢ *Liquid Biopsy: A Promising Approach for Oral Cancer Diagnosis and Treatment*

Liquid biopsy, a non-invasive technique that analyses biological materials in bodily fluids, is emerging as a powerful tool for early cancer detection, monitoring disease progression, and predicting treatment response. By examining biomarkers such as circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and extracellular vesicles (EVs), liquid biopsy offers a real-time window into the tumor's genetic and molecular landscape. In the context of oral cancer, liquid biopsy holds significant promise. By analyzing biomarkers like miRNAs, proteins, and genetic mutations in blood, saliva, or urine, clinicians can gain valuable insights into the tumor's behavior and identify potential therapeutic targets. However, while research has shown promising results, several challenges remain, including the need for larger and more diverse patient cohorts, standardization of methodologies, and validation in clinical settings. Despite these challenges, liquid biopsy has the potential to revolutionize oral cancer diagnosis and treatment. By enabling earlier detection, more accurate diagnosis, and personalized treatment strategies, liquid biopsy could significantly improve patient outcomes and reduce mortality rates associated with this disease. As research continues to advance, liquid biopsy is poised to become an indispensable tool in the fight against oral cancer.8,9

➢ *Saliva-as Tool for Diagnosis*

Saliva, being a biologically rich medium, contains a variety of biomarkers—proteins, RNA, and DNA—that can aid in the detection of oral cancer (OSCC). To date, over 100 potential biomarkers have been identified, opening new avenues for non-invasive oral cancer diagnosis. Among these biomarkers, microRNAs (miRNAs) have emerged as promising candidates. Specific miRNAs, including miRNA-9, miRNA-191, miRNA-125a, and miRNA-200a, have been found to exhibit distinct expression patterns in head and neck cancers, and their levels correlate with the progression of OSCC. These miRNAs may serve as valuable indicators for early-stage detection and monitoring the disease's progression. Additionally, genetic markers such as the tumor suppressor gene p53 and its associated anti-p53 proteins have been implicated in various cancers, including oral cancers. The p53 gene plays a crucial role in regulating the cell cycle and preventing tumorigenic, and its mutations can lead to the development of OSCC. Other biomarkers, including CA15-3 and CA125, are associated with cancers beyond the oral cavity, such as breast, ovarian, and lung cancers, but their role in oral cancer diagnosis is also under investigation. These markers can provide additional diagnostic value and help in differentiating OSCC from other malignancies or benign conditions. Matrix metalloproteinase (MMPs), a group of enzymes involved in the degradation of extracellular matrix components, are also critical in tumor progression. MMPs contribute to various stages of cancer development, including cell proliferation, invasion, and metastasis. Studies have shown elevated levels of MMPs, such as MMP-1, MMP-2, MMP-9, MMP-10, and MMP-12, in the saliva of patients with OSCC. Salivary biomarkers have also proven helpful in distinguishing OSCC from other oral conditions, such as benign lesions or oral potentially malignant disorders (OPMDs), like leukoplakia. These biomarkers can provide insights into the likelihood of malignant transformation, which is crucial for early intervention and preventive care. Inflammatory proteins like IL-6, IL-8, IL-1, and TNF-α, along with cell-surface glycoproteins like CD44, CD59, and CEA, have been extensively studied for their roles in OSCC. In addition to these well-established markers, non-targeted proteomic studies have identified additional proteins that hold promise for OSCC diagnosis. Proteins like M2BP, MRP14, CD59, catalase, and profilin have demonstrated high sensitivity and specificity in detecting OSCC, making them valuable additions to the growing list of salivary biomarkers. The ongoing research into these proteins could lead to more accurate and reliable diagnostic tests. Recent studies have also explored the potential of metabolic markers and glycoproteins, such as fucose and sialic acid, in diagnosing and monitoring OSCC. These markers are involved in cellular metabolism and glycosylation processes, which are often altered in cancer cells.12,13,14, 17,18

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➢ *Chemiluminescence*

Chemiluminescence, the light emitted during a chemical reaction, has long fascinated scientists, from ancient Chinese literature documenting firefly bioluminescence to Henning Brand's pioneering work in 1669. In the field of oral oncology, Chemiluminescence has become a promising non-invasive optical technique for early cancer detection, particularly in identifying dysplastic and neoplastic tissues in the oral cavity. The procedure involves rinsing the mouth with a 1% acetic acid solution, which acts as a cytoplasmic dehydrator, clearing debris, and breaking down the glycoprotein barrier on the epithelial surface. The subsequent activation of aspirin and hydrogen peroxide in the Vizilite capsule triggers a chemical reaction that emits a blue-white light (430–580 nm) for about 10 minutes. Under this chemiluminescent light, normal mucosa appears blue, while dysplastic and neoplastic tissues present a distinct "acetowhite" appearance due to altered light refractile properties. The advantages of this technique include early detection, enabling prompt intervention and potentially improving patient outcomes, as well as being non-invasive and providing real-time results during examinations, making the diagnostic process more efficient. Additionally, it is easy to perform, suitable for chair-side tests, and shows limited operator variability, reducing inconsistent results. However, there are limitations, including the high cost of devices and consumables, the need for a darkened environment for accurate visualization, and the inability to precisely indicate the biopsy site, requiring further investigation. Chemiluminescence has several applications, including as an adjunct to traditional oral mucosal examinations for oral cancer screening, improving the identification and follow-up of high-risk lesions. It is also used in the Vizilite Plus system, which combines chemiluminescence with toluidine blue marking for enhanced lesion visualization and delineation for biopsies.10, 19

➢ *Brush Biopsy*

Brush biopsy, also known as oral brush cytology or Oral CDx, is a non-invasive diagnostic technique used to detect precancerous or malignant oral mucosal lesions. This method involves using a specialized brush to collect cells from the oral epithelium, which are then analyzed for abnormalities. It is an important tool for the early detection and screening of oral cancer, particularly in high-prevalence regions like developing countries. The technique utilizes a stiff bristle brush designed to penetrate the oral mucosa's thickness. The brush is rotated on a suspicious lesion until it produces bleeding or reddening, ensuring that a representative sample from all epithelial layers, including basal, intermediate, and superficial, is collected. The sample is then fixed and sent to the lab for analysis using computer-based imaging systems, and results are reported as negative (no abnormalities), atypical (uncertain changes), positive (evidence of dysplasia or carcinoma), or inadequate (incomplete sample). One of the main advantages of brush biopsy is that it is non-invasive, well-accepted by patients, and less painful than traditional biopsy methods. It aids in the early detection of precancerous lesions and oral cancer, improving treatment outcomes and survival rates. The procedure is relatively simple, quick, and requires minimal training, making it easy for oral health professionals to perform chair-side. It also causes less bleeding than traditional scalpel biopsies and is a cost-effective alternative, particularly for low-risk patients. However, there are limitations, including the need for a second procedure, such as a scalpel biopsy, if the results are atypical or positive, which can delay diagnosis. The technique may also provide indeterminate results in some cases, necessitating further investigation. Additionally, certain lesions may be difficult to diagnose with this method, requiring expertise in cytological interpretation. Brush biopsy has various applications, such as the early detection of oral cancer, screening high-risk patients with red or white spots, chronic ulcers, or abnormal epithelial lesions, evaluating small or suspicious lesions not visible during clinical examination, and monitoring changes in precancerous lesions over time to guide treatment decisions.14

III. INNOVATIVE IMAGING TECHNIQUES

Innovative imaging techniques have significantly advanced the detection and diagnosis of oral cancer, offering non-invasive, real-time methods for identifying abnormal tissue changes. Autofluorescence imaging devices, such as VELscope and Identify, utilize fluorescence to detect abnormal tissue in the oral cavity, highlighting potentially precancerous and cancerous lesions that might not be visible to the naked eye. These devices enhance the clinician's ability to identify early-stage oral cancer, improving the chances of timely intervention. Raman spectroscopy is another cutting-edge technology that measures molecular differences between healthy and malignant tissues by analyzing the scattering of light, providing a non-invasive, real-time diagnostic tool. This technique can detect chemical signatures specific to cancerous tissues, offering a potential alternative to traditional biopsy methods. Optical Coherence Tomography (OCT) and Confocal Laser Endomicroscopy (CLE) are high-resolution, real-time imaging technologies that allow the detection of microstructural changes in oral lesions, such as alterations in tissue architecture or cell structure, that may indicate early malignancy. OCT provides detailed cross-sectional images of tissue, while CLE allows for live visualization of tissue at a cellular level. Both technologies aid in the early-stage diagnosis of oral cancer by offering a more comprehensive understanding of tissue changes, thus enhancing the ability to differentiate between benign and malignant lesions and guiding appropriate treatment decisions. Together, these imaging innovations offer promising tools for improving the early detection and management of oral cancer, ultimately contributing to better patient outcomes.15,16

➢ *Nano Diagnostics*

Nano diagnostics, defined as the use of nanotechnology for clinical diagnostic purposes, was developed to meet the demands of clinical diagnostics for increased sensitivity and earlier detection of disease. The integration of nanotechnologies in diagnostic applications holds tremendous potential for meeting the stringent requirements of clinical laboratories in terms of sensitivity and cost-effectiveness. Recent advancements have led to the development of innovative nano-diagnostic tools, including quantum dots (QDs), gold nanoparticles, and cantilevers. Quantum dots, in particular, have emerged as the most promising nanostructures for diagnostic applications, boasting exceptional photostability, single-wavelength excitation, and size-tunable emission properties. Furthermore, quantum dots and magnetic nanoparticles can be leveraged for the barcoding of specific analytes. The bio-barcode assay, which incorporates gold and magnetic nanoparticles, has been proposed as a potential alternative to polymerase chain reaction (PCR). The diagnostic applications of quantum dots are vast and varied, with the most promising uses being in tumor detection, tissue imaging, intracellular imaging, immunohistochemistry, infectious agent detection, multiplexed diagnostics, and fluor immunoassays. Nano diagnostics promise increased sensitivity, multiplexing capabilities, and reduced cost for many diagnostic applications as well as intracellular imaging. 20.

IV. CONCLUSION

In conclusion, while these advancements in imaging techniques and non-invasive diagnostic methods represent significant progress, challenges still remain in their clinical validation. To ensure their widespread adoption and effectiveness across diverse populations, large-scale studies and rigorous clinical trials are essential. These studies will be crucial in confirming the reliability, accuracy, and feasibility of these technologies in real-world clinical settings. Additionally, it is important to address factors such as cost-effectiveness, accessibility, and standardization to make these innovative tools available to a broader range of healthcare facilities and patients. By overcoming these challenges, these advancements have the potential to revolutionize the early detection, diagnosis, and management of oral cancer, ultimately leading to improved patient outcomes and survival rates.

REFERENCES

[1]. Venkatesh g. Naikmasur, Atul P Sattur, Sunil Mutalik, Arpita rai Thakur, Journal of Indian Academy of Oral medicine and radiology. DOI : 10.4103/0972-1363.58748.
[2]. Chakraborty D., Natarajan C., Mukherjee A. Advances in Oral Cancer Detection. Adv. Clin. Chem. 2019;91:181–200. Doi: 10.1016/bs.acc.2019.03.006.
[3]. By Antenne Vistoso Monreal DDS, MS, DABOP and Amalia Arutiunian, DDS, Herman Ostrow of Dentistry of USC.
[4]. Mayra, Alejandra, Dávila, Olivos., Henry, Miguel, Herrera, Del, Águila., Félix, Melchor, Santos, López. (2024). 4. Diagnosis of oral cancer using deep learning algorithms. Ingenius: Revista de Ciencia y Tecnología, doi: 10.17163/ings.n32.2024.06
[5]. Khanagar SB, Alkadi L, Alghilan MA, Kalagi S, Awawdeh M, Bijai LK, Vishwanathaiah S, Aldhebaib A, Singh OG. Application and Performance of Artificial Intelligence (AI) in Oral Cancer Diagnosis and Prediction Using Histopathological Images: A Systematic Review. Biomedicines. 2023 Jun 1;11(6):1612. doi: 10.3390/biomedicines11061612. PMID: 37371706; PMCID: PMC10295336.
[6]. Poonia M, Ramalingam K, Goyal S, Sidhu SK. Nanotechnology in oral cancer: A comprehensive review. J Oral Maxillofac Pathol. 2017 Sep-Dec;21(3):407-414. Doi: 10.4103/jomfp.JOMFP_29_17. PMID: 29391716; PMCID: PMC5763864.
[7]. Ravindran R. Nano technology in cancer diagnosis and treatment: An overview. Oral Maxillofac Pathol J. 2011;2:101–6.
[8]. Naito Y, Honda K. Liquid Biopsy for Oral Cancer Diagnosis: Recent Advances and Challenges. J Pers Med. 2023 Feb 8;13(2):303. Doi: 10.3390/jpm13020303. PMID: 36836537; PMCID: PMC9960348.
[9]. Ignatiadis M., Sledge G.W., Jeffrey S.S. Liquid biopsy enters the clinic—Implementation issues and future challenges. Nat. Rev. Clin. Oncol. 2021;18:297– 312. Doi: 10.1038/s41571-020-00457-x.
[10]. Hu S, Arellano M, Boontheung P, et al. Salivary proteomics for oral cancer biomarker discovery. Clin Cancer Res 2008;14(19):6246–52
[11]. Oriana, Barros., Vito, G, D'Agostino., Lúcio, Lara, Santos., Rui, Vitorino., Rita, Ferreira. (2024). 6. Shaping the future of oral cancer diagnosis: advances in salivary proteomics.. Expert Review of Proteomics, doi: 10.1080/14789450.2024.2343585
[12]. Tahereh, Nosratzehi., Shahin, Nosratzehi. (2024). 10. Oral cancer and salivary biomarkers in its early diagnosis: A review of literature. Journal of Medical Society, doi: 10.4103/jms.jms_90_23
[13]. Piyush, Bhati., Tassaduq, Hussain, Wani., Deepti, Kaushik., Kanu, Priya., Mohd, Ashraf. (2024). 10. Oral Cancer and Prospects of Precision Medicine. Doi: 10.2174/9789815223583124010018
[14]. Shafia, Rahman., Dr, SyedaArshiya, Ara. (2024). 6. Recent advances in diagnostic oral medicine. Doi: 10.58532/v3bfms7p1ch5
[15]. Sneha, Sahani., Semanti, Ghosh., Bidisha, Ghosh. (2024). 9. Oral cancer: Advances in diagnosis and treatment of oral cancer using biomarkers and marine algal drugs.
[16]. International journal of oncology research, doi: 10.33545/2664665x.2024.v4.i1a.11
[17]. Piyush, Bhati., Tassaduq, Hussain, Wani., Deepti, Kaushik., Kanu, Priya., Mohd, Ashraf. (2024). 10. Oral Cancer and Prospects of Precision Medicine. Doi: 10.2174/9789815223583124010018
[18]. Mohammad A Javaid, Ahad s Ahmed, Robert Durand, Simon D Tran, J Oral Biol Craniofac Res. 2015 Sep 9;6(1):66–75. Doi: 10.1016/j.jobcr.2015.08.006

[19]. Chen-Zi Zhang,Xing-Qun Cheng,Ji-Yao Li,Ping Zhang,Ping Yi,Xue-Dong Zhou International Journal of Oral Science
[20]. Marina A Tzani ,Dimitra K Gioftsidou, Michael G Kallitsakis, Nikolaos V Pliatsios, Natasa P Kalogiouri, Panagiotis A Angaridis, Ioannis N Lykakis, Michael A Terzidis Molecules. 2021 Dec 17;26(24):7664. Doi: 10.3390/molecules26247664, National Library of Medicine
[21]. Khalid Khalaf Alharbi, Yazeed A Al-sheikh, Saudi J Biol Sci. 2013 Nov 19;21(2):109–117. Doi: 10.1016/j.sjbs.2013.11.001, National Library of Medicine